

Appl. No. 09/751,962  
Amendment dated June 4, 2003  
Reply to Office Action of December 4, 2002

## **REMARKS**

Applicant has received and reviewed an Office Action dated December 4, 2002. By way of response, Applicant has amended the specification to correct a typographical error in the brief description of Figures 1 and 2. No new matter is presented. Claims 1-69 are pending. Applicant submits that the pending claims are supported by the specification.

For the reasons given below, Applicant submits that the amended claims are in condition for allowance and notification to that effect is earnestly solicited.

### **Petition for Extension of Time**

It is noted that a 3-month petition for extension of time is necessary to provide for timeliness of the response. A request for such an extension is made extending the time for response from March 4, 2003 to June 4, 2003.

### **Oath/Declaration**

The Examiner suggests that the oath or declaration is defective because: it appears as if the declaration was signed in 1978.

First, Applicant notes that the oath was acceptable in the parent case and that an oath from a parent case is suitable for use in a continuation application. Second, Applicant believes that it is reasonable to assume that Dr. Catcheside wrote a "9" with the loop squished. Third, Applicant notes that the MPEP at 602.05 indicates that the Office no longer checks the date of execution of the oath or declaration. Fourth, the MPEP at 602.05(a) lists the requirements for an oath or declaration in a continuation or divisional application and makes no reference to correcting the date of execution of the oath or declaration.

Consequently, Applicant believes that the copy of the oath taken from the parent case is acceptable in this continuation application. Applicant respectfully requests withdrawal of this objection to the oath or declaration.

**Specification**

Applicant thanks the Examiner for his attention to detail in noting a beneficial correction to a typographical error in the specification. The present amendment provides the correction requested by the Examiner. No new matter was added by this amendment.

**Rejection of Claims Under § 112, First Paragraph**

The Examiner rejected claims 1-3, 8-36, and 42-69 under 35 U.S.C. § 112, first paragraph. The Examiner asserts that the specification does not fully describe all recombination hotspots. Applicant respectfully traverses this rejection.

**The Presently Claimed Invention**

Applicant respectfully submits that the specification need not fully describe all recombination hotspots, because the pending claims recite cells including eukaryotic hotspots (Amendment and Response mailed August 26, 2002).

The presently claimed invention relates to new and nonobvious cells including a new and nonobvious recombinant genome. This recombinant genome includes a new and nonobvious combination of two known features, heterologous DNA and an eukaryotic recombination hotspot. Any of a variety of known eukaryotic recombination hotspots can be employed in the claimed cells. The cells are new and nonobvious, numerous eukaryotic recombination hotspots are known and described in the present application.

Further, the claims of the present continuation application represent only a modest increase in breadth compared to the issued and valid claims of US Patent No. 6,232,112 (the '112 patent). Claims 68 and 69 of the '112 patent relate to cells including fungal recombination hotspots. The present application merely seeks to expand the claim coverage from cells including recombination hotspots of one representative group of eukaryotes (fungi) to cells including hotspots of eukaryotes in general. The present application fully supports and describes this additional scope for the claims.

**The Present Specification Adequately Describes a Representative Number of Eukaryotic Hotspots**

The Office Action correctly notes that claims reciting eukaryotic hotspots can be adequately described by disclosure of a representative number of eukaryotic hotspots including a combination of identifying characteristics sufficient to show Applicant was in possession of the eukaryotic hotspots. Applicant respectfully submits that the present application more than satisfies this requirement.

At the filing date of the parent application, numerous eukaryotic hotspots were known to those of skill in the art. The present application refers to numerous of these known eukaryotic hotspots in sufficient detail to inform one of skill in the art that Applicant was in possession of them. For example, the present application describes by organism and location eukaryotic hotspots including:

- 1) *Saccharomyces cerevisiae* at the *arg4* loci (M Lichten and ASH Goldman Ann. Rev. Genet. 29: 423-444 1995)
- 2) *Saccharomyces cerevisiae* at the *his4* loci (M Lichten and ASH Goldman Ann. Rev. Genet. 29: 423-444 1995)
- 3) *N. crassa* at *cog*
- 4) *N. crassa* at *am* loci
- 5) *N. crassa* at *his-3* loci
- 6) at mating type loci in the Basidiomycete *Schizophilum commune* (G Simchen and J Stemberg Heredity 24: 369-381 1969)
- 7) 5' of *cys3* in *S. cerevisiae*,
- 8) 5' of *his2* in *S. cerevisiae*,
- 9) *Schizosaccharomyces pombe* within the *ade6* gene
- 10) *Schizosaccharomyces pombe* 5' of the *ade6* gene
- 11) at *his-1* in *Neurospora crassa*
- 12) at *nit-2* in *Neurospora crassa*
- 13) near *pyr-3* in *Neurospora crassa*
- 14) near *sn* in *Neurospora crassa*
- 15) near *his-2* in *Neurospora crassa*
- 16) hotspots in the fungi *Aspergillus nidulans*
- 17) hotspots known to exist in the fungi *Schizophillum commune*

- 18) HOT1 in the genome of *Saccharomyces cerevisiae*.
- 19) in maize
- 20) mouse (*Mus musculus*) - close to the major histocompatibility locus
- 21) human (*Homo sapiens*) - near the gamma globulin loci
- 22) Chimpanzee - near the gamma globulin loci
- 23) in humans near the retinoic acid alpha receptor gene
- 24) in humans in the region of the repeat sequences associated with Charcot-Marie-Tooth neuropathy

These eukaryotic hotspots are described in the specification at least at page 6, line 22, through page 7, line 11, and at page 20, lines 10-27. The present application describes these eukaryotic hotspots by citation to the scientific literature, as "directly demonstrated", as having been "studied", as "known to exist", as "found in", as "known", and the like. Id. These well known and described eukaryotic hotspots include representatives from fungi, mammals (including humans), and plants.

The Office Action correctly suggests that scientific publications from the time of the parent application can inform the skilled worker of the adequacy of the application's written description. In the present situation, scientific publications indicate that the specification's recitation of locations (or loci) and organisms was adequate to place the reader in possession of the eukaryotic hotspots. For example, the following table provides citations to references in the scientific literature relating to characterization of numerous of the 24 eukaryotic hotspots described in the present patent application. These references indicate that these eukaryotic hotspots were known and well-characterized in the scientific literature before filing of the present patent application. Applicant did not have to characterize these hotspots. These eukaryotic hotspots include representatives from fungi, insects, mammals (including humans), and plants.

Gene	Organism	Citation
<b>YEAST</b>		
ade6	<i>S. pombe</i>	Genetics 119: 491 -7 1988, EMBO 13: 5121-9 1994, Genetics 136: 41-51 1994, Genetics 141: 33-48 1995
ura-4	<i>S. pombe</i>	Genetics 140: 469-78 1995
ampR	<i>S. cerevisiae</i>	Genetics 127: 39-51 1991

<b>Gene</b>	<b>Organism</b>	<b>Citation</b>
HIS4	<i>S. cerevisiae</i>	PNAS: 90: 6621-5 1993
BIK1	<i>S. cerevisiae</i>	Genetics 134 5-19 1993
HIS2	<i>S. cerevisiae</i>	Genetics 144: 71-86 1996
	<b>PLANT</b>	
	<i>L. esculentum</i> (tomato)	Plant Cell 9: 1633-1646 1996
wx	<i>Z. mays</i> (maize)	Genetics 147: 815-21 1997
bz1 & bz2	<i>Z. mays</i>	Plant Cell 9: 1633-46 1997
	<b>INSECT</b>	
Tpl	<i>D. melanogaster</i> (fruitfly)	Genetics 122: 397-401 1989
	<b>MAMMAL</b>	
	<i>M. musculus</i> (mouse)	Cell 57: 937-46 1989
beta 2&3	<i>M. musculus</i>	Immunogenetics 31: 79-88 1990, EMBO 10: 681-6 1997
Eb	<i>M. musculus</i>	Mammalian Genome 2: 123-9 1992
Lmp-2	<i>M. musculus</i>	Advances in Biophysics 31: 119-32 1995, Mammalian Genome 7: 490-6 1996
bcl-2	<i>H. sapiens</i> (human)	International Immunology 7: 1191-204 1995
TAP2	<i>H. sapiens</i>	J Human Genetics 56: 1350-8 1995
	<i>H. sapiens</i>	Nature Genetics 12: 288-97 1996
MHC1B	<i>H. sapiens</i>	Immunogenetics 46: 499-508 1997

The description of the organism and location provided in the application together with the knowledge present in the scientific literature at the filing date of the invention would put the skilled worker in possession of these eukaryotic hotspots. These hotspots provide a representative sampling of eukaryotic hotspots.

This description of eukaryotic hotspots together with the remaining extensive disclosure of this patent application fully describes the presently claimed cells.

Accordingly, the present claims fully comply with § 112, first paragraph, and withdrawal of this rejection is respectfully requested.

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**Obviousness-Type Double Patenting Rejection**

The Examiner rejected claims 1-69 under the judicially created doctrine of obviousness-type double patenting as obvious over claims a 1-67 of U.S. Patent No. 6,232,112. Applicant respectfully traverse is this rejection.

Nonetheless, solely to expedite prosecution of this application and not to acquiesce to the rejection, Applicant submits herewith a terminal disclaimer obviating this rejection.

Accordingly, Applicant respectfully requests withdrawal of this rejection.

**Summary**

In summary, each of the pending claims 1-69 is in condition for allowance. The Examiner is invited to contact Applicant's undersigned representative and the telephone number listed below, if the Examiner believes that doing so will advance prosecution of this application.

Respectfully submitted,

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